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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/822,677	04/13/2004	Richard J. Davis	620-301	3671

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EXAMINER	
NICHOLS, CHRISTOPHER J	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 04/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/822,677	DAVIS ET AL.	
	Examiner	Art Unit	
	Christopher J. Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *1,3,5,7,9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,6 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-10* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/897412.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4.13.04*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Preliminary Amendment filed 13 April 2004 has been received and entered in full.

Election/Restrictions

2. Applicant's election of Group II (claims **2, 4, 6,** and **8**) in the reply filed on 22 February 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims **1, 3, 5, 7,** and **9-10** are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 22 February 2005.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims **2, 4, 6,** and **8** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *a method of treatment of chronic obstructive pulmonary disease (COPD) in a patient suffering from COPD, the method comprising administering to said patient an effective amount of a secretin receptor ligand or the polypeptide of the SEQ ID NO: 10 sequence, wherein said a secretin receptor ligand or the polypeptide of the SEQ ID NO: 10*

sequence triggers anion efflux in respiratory tissue via activation of a secretin receptor, does not reasonably provide enablement for *use of other agents*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to **make** or **use** the invention commensurate in scope with these claims.

5. The claims are drawn very broadly to a method of treating chronic obstructive pulmonary disease (COPD) using any agent which triggers anion efflux in respiratory tissue via the activation of a secretin receptor. The language of said claims encompasses any given agent which activates a secretin receptor.

6. The specification teaches that the clinical features of chronic obstructive pulmonary disease (COPD) include breathlessness, cough and sputum, chronic airway obstruction and lung hyperinflation as a result of chronic bronchitis and emphysema.

7. A bronchodilator regimen combining a slow release oral theophylline with an inhaled beta 2 agonist (e.g. ipratropium, salbutamol, salmeterol), and high dose inhaled steroids are the current therapies for COPD. Even modest improvement in obstruction is beneficial in COPD patients.

8. The secretin receptor is a GPCR and its ligand, secretin, stimulates water and bicarbonate secretion from the pancreas. Vasoactive intestinal peptide (VIP), PACAP (pituitary adenylate cyclase-activating polypeptide), glucagon, and glucagon-like peptide (GLP) are all structurally similar to secretin and act as ligands of the sercretin receptor (pp. 14).

9. The specification fails to provide any guidance for the successful manufacture and use of any agents other than secretin receptor ligands and the polypeptide of SEQ ID NO: 10. Since resolution of the various complications in regards to identifying and characterizing a therapeutic

agent are highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of formulations of new agents to correlate with treatment of COPD. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

10. Additionally, a person skilled in the art would recognize that predicting the efficacy of using therapeutic based solely a target and desired activity as highly problematic (see MPEP §2164.02). Thus, although the specification prophetically considers and discloses general methodologies of using the any given secretin receptor binding agents, such a disclosure would not be considered enabling since the state of therapeutic compounds for COPD is highly unpredictable and complex. The factors listed below have been considered in the analysis of enablement [see MPEP §2164.01(a) and *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)]:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

11. The following references are cited herein to illustrate the state of the art of COPD.

12. On the nature of the invention, Paolo *et al.* (July 1999) "Properties of a Recombinant Human Secretin Receptor: A Comparison with the Rat and Rabbit Receptors." Pancreas **19**(1): 51-55 teaches that porcine secretin, human secretin, rabbit secretin, VIP, and secretin derivatives all differ in their affinity for rat, rabbit, and human secretin receptors (Table 2). Thus the claims as instantly presented encompass a large and unpredictable genus of agents.

13. Thus the specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of applying results from *prophetic* guidance to the *treatment of COPD* as exemplified in the references herein.

14. Claim **1** is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

15. The claim requires "an agent which triggers anion efflux in a respiratory tissue via the activation of a secretin receptor" but does not require that the agent to possess any particular conserved structure. Furthermore the art recognizes that "agent" can pertain to chemical entities, pharmaceutical compositions, proteins, peptides, non-peptide compounds, animal tissue extracts, nucleic acids, antisense molecules, peptidomimetic, transformed cells, antibodies, antibody fragments, cyclic peptides, agonists, antagonists, inhibitors, enhancers, vegetable extracts, cell extracts, synthetic agents, biologically derived substances as well as proteinaceous substances, known, and unknown compounds.

16. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus.

The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a recitation of *desired biological activity in the absence of structural limitations*. The specification does not identify any particular portion of the structure that must be conserved, nor does it provide a disclosure of structure/function correlation. The distinguishing characteristics of the claimed genus are not described. Accordingly, the specification does not provide adequate written description of the claimed genus.

17. To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563; see also *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); *In re Gosteli*, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572.

18. See *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 (DC WNY 2003) and *University of Rochester v. G.D. Searle & Co. et al.* CAFC [(03-1304) 13 February 2004]. In

University of Rochester v. G.D. Searle & Co. wherein the court rejected: "a patent directed to method for inhibiting prostaglandin synthesis in a human host using an unspecified compound, in order to relieve pain without the side effect of stomach irritation, did not satisfy the written description requirement of 35 U.S.C. §112, since the patent described the compound's desired function of reducing the activity of the enzyme PGHS-2 without adversely affecting PGHS-1 enzyme activity, but did not identify said compound, since the invention consists of performing 'assays' to screen compounds in order to discover those with the desired effect, but the patent did not name even one compound that assays would identify as suitable for practice of the invention, or provide information such that one skilled in art could identify any suitable compounds, since the specification did not indicate that compounds are available in public depository, since claimed treatment method cannot be practiced without the compound, and since inventors thus cannot be said to have 'possessed' the claimed invention without knowing of the compound or a method certain to produce the compound." Thus said patent constituted an invitation to experiment to first identify, then characterize, and the use a therapeutic a class of compound defined only by their desired properties. Thus said patent constituted an invitation to experiment to first identify, then characterize, and then use a therapeutic a class of compound defined only by their desired properties.

19. Therefore the full breadth of the claim fails to meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims **2** and **4** are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/02453 (22 January 1998) (**IDS**).

21. WO 98/02453 teaches a method of treating COPD comprising administering a secretin peptide thus meeting the limitations of claims 2 and 4 (pp. 1, 3, 8 lines 18-30; Figure 1). WO 98/02453 encompasses all the ligands taught therein by the generic claim 1 are known as secretin analogues (pp. 14-15 and Table1). Since claim 4 asserts that a secretin receptor ligand would meet the limitations of "an agent which triggers anion efflux in respiratory tissue via the activation of a secretin receptor", the porcine and rabbit secretin peptides taught by WO 98/02453 meet these ligands because a compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. Claims **2, 4,** and **8** rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/02453 and Chien and Chang (1987) "Intranasal drug delivery for systemic medications." Crit Rev Ther Drug Carrier Syst. **4**(2): 67-194.

23. WO 98/02453 teaches a method of treating COPD comprising administering a secretin peptide thus meeting the limitations of claims 2 and 4 (pp. 1, 3, 8 lines 18-30; Figure 1). WO 98/02453 encompasses all the ligands taught therein by the generic claim 1 (pp. 14-15 and Table1). Since claim 4 asserts that a secretin receptor ligand would meet the limitations of "an agent which triggers anion efflux in respiratory tissue via the activation of a secretin receptor", the porcine and rabbit secretin peptides taught by WO 98/02453 meet these ligands because a compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)).

24. WO 98/02453 does not teach, however, inhalation (intranasal) administration.

25. Chien and Chang (1987) teach that intranasal (inhalation) administration has advantages: (a) avoidance of hepatic first-pass elimination, gut wall metabolism, and/or destruction in gastrointestinal fluids; (b) the rate and extent of absorption and the plasma level-time profile is comparable to intravenous administration; (c) the rich vasculature and numerous microvilli structure in the nasal cavity offer a feasible and desirable site for absorption of systemically effective drugs (pp. 67).

26. Therefore it would have been obvious to a person of ordinary skill in the art at the time of the invention to combine the therapeutic method of WO 98/02453 with the delivery method of Chien and Chang (1987).

27. A person of ordinary skill in the art at the time of the invention would have been motivated to combine the therapeutic method of WO 98/02453 with the delivery method of Chien and Chang (1987) because of the advantages taught by Chien and Chang (1987).

28. A person of ordinary skill in the art at the time of the invention would have been have had a reasonable expectation of success because of the successfully examples as taught by Chien and Chang (1987) using inhalation (intranasal) therapies (pp. 117-121).

29. Thus the invention as a whole was *prima facia* obvious over the prior art.

Summary

30. No claims are allowed.

31. The Examiner notes that secretin, glucagons, VIP, peptide histidine isoleucine, GIP, GHRF, and PACAP are all secretin ligands [see Dong & Miller (2002) "Molecular Pharmacology of the Secretin Receptor." Receptors and Channels **8**: 189-200 (pp. 190)].

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is **(571) 272-0889**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback** can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

CJN
March 31, 2005